1812 #17 W 9/8/93

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of :

Wolfgang R. STREBER et al. : Group Art Unit: 1812

Serial No.: 07/322,604 : Examiner: J. Ulm

Filed: March 10, 1989 :

For: **MICROORGANISMS AND PLASMIDS FOR 2,4-DICHLOROPHENOXYACETIC ACID (2,4-D) MONOOXYGENASE FORMATION AND PROCESS FOR THE PRODUCTION OF THESE PLASMIDS AND STRAINS**

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REPLY BRIEF

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

SIR:

This paper is responsive to the Examiner's Answer dated November 12, 1992. Being filed herewith is appellants' Reply Brief in triplicate. The Commissioner is hereby authorized to charge the statutory fee of $110.00 for a one-month extension of time to counsel's Deposit Account No. 13-3402; two copies of this page being attached for this purpose.

New Points of Argument

The allegation that the specification only enables isolation of a 2,4-D-monooxygenase gene from a bacteria able to utilize 2,4-D as a sole carbon source is erroneous.

In the paragraph bridging pages 6-7 of the Examiner's Answer, the Examiner alleges that the specification only enables isolation of a 2,4-D-monooxygenase gene from a bacteria able to utilize 2,4-D as a sole carbon source. This analysis is erroneous, and improperly characterizes the invention.

In fact, the specification describes, inter alia, a method of identifying transformed bacterial **recipient hosts** of the gene

isolated from a donor organism containing the gene, which method involves the ability of the host to use 2,4-D as a sole carbon source. However, this method identifies transformed **recipients** capable of converting 2,4-D or phenoxyacetic acid to the corresponding phenol through their ability to use the phenol as a sole carbon source. It is not the donor organism which is required to have the ability to utilize 2,4-D as a sole carbon source. Since the gene, after being transformed into the recipient host, is under very different regulatory conditions, this is an important distinction.

Furthermore, the Examiner's statement that the method applicable to identifying sequences isolatable from bacteria able to use 2,4-D as a sole carbon source "would undoubtedly exclude organisms able to use 2,4-D as an ancillary carbon source" is factually incorrect and misleading. Even if the statement were true (which it most definitely is **not**, in view of the discussion above), at best what could be meant is that a method of identification of bacteria containing the gene based upon an identification technique using the ability to use 2,4-D as a sole carbon source **could** miss organisms **only** able to use 2,4-D as an ancillary carbon source. Nevertheless, this distinction is meaningless, since the method of identification is in fact performed on the recipient hosts, wherein the gene is in a different regulatory environment, and the entire argument is incorrect on its face.

The characterization of the similarity of the herbicide resistance gene taught by Comai et al. with the 2,4-D monooxygenase gene of the present invention is misleading.

The mere allegation by the Examiner that the structural gene transferred in Comai et al. confers herbicide resistance and is structurally distinct from the corresponding plant gene which is poisoned by the herbicide glyphosate does not refute the main thrust of Appellants' rebuttal analysis of the teaching of the reference, which rebuttal is respectfully submitted to have overcome any possible prima facie case. While the Examiner's statements are factually correct, as far as they go, they fail to address the primary difference between the teaching of the

reference and the present invention. Furthermore, they fail to counter the Appellants' rebuttal arguments that the deficiencies of the teaching of the reference evidence the lack of motivation a skilled worker would have had for combining the references to arrive at the present invention.

As was argued in the Brief on Appeal, glyphosate is an herbicide by means of poisoning a vital metabolic enzyme in the plant. The Comai et al. reference teaches transferring into the plant a bacterial gene resistant to glyphosate which replaces the poisoned plant enzyme. In contrast, the present invention provides plants with a means of detoxifying the herbicide 2,4-D by metabolizing it to a less toxic phenolic compound. However, plants do not normally have the ability to perform this reaction, and the resultant phenols are known to be toxic to plants as well. This is a very different means of "providing herbicide resistance."

Even though the bacterial structural gene *aroA* is alleged by the Examiner (with no evidence provided) to be structurally unrelated to the corresponding plant EPSP synthase gene, it still codes for an enzyme which performs the same reaction as the plant EPSP synthase, and the reaction product is the same as that produced by the indigenous gene, which is therefore clearly not toxic to the plant. In contrast, in the present invention, the new gene does not have a plant counterpart, and the enzyme it encodes produces a toxic phenol from the even more toxic herbicide starting compound. Therefore, although the reference generically teaches a method of conferring herbicide resistance in plants by transferring into the plant a bacterial gene, the teaching of the reference does not provide motivation to arrive at the present invention because the mechanisms of achieving herbicide resistance are so different.

Furthermore, even assuming, arguendo, that a method of conferring herbicide resistance by replacing a poisoned indigenous gene with an analogous bacterial gene renders obvious a method of conferring herbicide resistance by introducing a completely foreign gene having a completely new biological activity (which is obviously not conceded), there would be no way to predict from the

teaching of the reference whether such a foreign gene would be compatible with life in a plant cell. Therefore, the Examiner's argument is still insufficient to reestablish a prima facie case in view of Appellants' previous rebuttal arguments, even assuming one ever properly existed.

In view of the above remarks, it is respectfully requested that the Board of Appeals **reverse** the rejections of the various claims and pass the application to issue.

Respectfully submitted,

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